Role of multidrug-resistant pathogens in health-care-associated pneumonia

We read with interest Santiago Ewig and colleagues' article[1] discussing the validity of a new classification scheme for pneumonia, including for health-care-associated pneumonia (HCAP). The investigators reviewed the available evidence, including our 2009 study.[2] They conclude that this study does not prove much more than that patients admitted to hospital within 180 days have a similar mortality as patients with hospital-acquired pneumonia, and that the key issue of HCAP—excess mortality due to drug-resistant pathogens—was not assessed. Here we present microbiological data from this prospective study, which was undertaken in Italy between January and July, 2007.

Microbiological data were culture results from the first 5 days after admission to hospital, or within 5 days of diagnosis with pneumonia. An aetiological diagnosis was definitive if one of the following criteria were met: (1) blood cultures yielded a bacterial pathogen (in the absence of an apparent extrapulmonary focus); (2) pleural fluid and cultures of transthoracic needle aspiration yielded a bacterial pathogen; (3) a respiratory sample that was representative of the lower respiratory tract (fiberoptic bronchoscopy with protected catheter) yielded a bacterial pathogen; (4) isolation of *Legionella pneumophila* in sputum, or detection of *L pneumophila* serogroup 1 or pneumococcal antigen in urine; (5) an increase of four times in the antibody titre, or seroconversion for atypical pathogens. An aetiological diagnosis was regarded as presumptive when a predominant microorganism was isolated from a purulent sample (more than 25 polymorphonuclear leucocytes and fewer than ten squamous cells per low-power field [original magnification×10]) with compatible findings from Gram stains.

Overall, an aetiological diagnosis was obtained in 22·4% of patients (95% CI 20·2–24·6). 28·4% (23·4–33·4) had a presumptive microbiological diagnosis, and 71·6% (66·6–77·6) a definitive diagnosis. Bacteraemia occurred in six patients with HCAP (*Streptococcus pneumoniae* in two, *Staphylococcus aureus* in three, and *Escherichia coli* in one), in four patients with hospital-acquired pneumonia (*S aureus* in three, and *E coli* in one), and in seven patients with community-acquired pneumonia (*S pneumoniae* in four, *E coli* in two, and *Pseudonomas aeruginosa* in one). No statistically significant differences were noted in the rates of bacteraemia between the three groups. A microbiological documentation was more frequently obtained in patients with HCAP (31·1%, 95% CI 19·7–42·5) than in those with community-acquired (18·4, 11·9–24·8) or hospital-acquired pneumonia (24·5, 9·2–39·8).

The distribution of pathogens varied among the three pneumonia categories (table), with *S aureus* predominating in the HCAP and hospital-acquired pneumonia groups, and *S pneumoniae* in the community-acquired group. The rate of meticillin resistance among *S aureus* isolates was 37·5% in the community-acquired group, 63·6% in the HCAP group, and 50% in the hospital-acquired group. These results seem to confirm the role of potentially multidrug resistant pathogens such as *S aureus, P aeruginosa,* and other Gram-negative bacilli, in patients with HCAP. As noted by other investigators,[3-5] patients with HCAP have a higher incidence of multidrug-resistant bacteria and, consequently, an increased likelihood of receiving inappropriate antibacterial therapy at the start.[2] This factor seems to be crucial in explaining the increased mortality recorded for HCAP.

In our study, features of patients with community-acquired pneumonia and HCAP were not substantially different in terms of median age, presence of comorbidities, or immunosuppression. Thus, the proposed classification of community-acquired pneumonia based on mean age or functional status is questionable. The review by Ewig and colleagues underestimates the value of clinical and microbiological studies undertaken in different areas of the world (Europe, Japan, and the USA). Future prospective clinical trials are needed to delineate the pathogens and risk factors associated with HCAP. However, the available evidence supports HCAP as a new category of pneumonia, which is distinct from community-acquired

	CAP n=41	HCAP n=28	HAP n=12	p value
Staphylooccus aureus	7 (17·1%)	11 (39·3%)	6 (50·0%)	0·034
Streptococcus pneumoniae	18 (43·9%)	2 (7·1%)	0	<0·001
Gram-negative bacteria				
Pseudonomas aeruginosa	4 (9·7%)	2 (7·1%)	2 (16·7%)	0·65
Enterobacteriaceae and other Gram negative bacilli	5 (12·2%)	9 (32·1%)	2 (16·7%)	0·11
Haemophilus influenzae/parainfluenzae	1 (2·4%)	1 (3·6%)	1 (8·3%)	0·68
Atypical bacteria				
Mycoplasma, Chlamydia, Legionella spp	3 (7·3%)	1 (3·6%)	1 (8·3%)	0·77
Others*†	3 (7·3%)	2 (7·1%)	0	0·69

Data are number (%) of patients. CAP=community-acquired pneumonia. HCAP=health-care-associated pneumonia. HAP=hospital-acquired pneumonia. *CAP: one atypical mycobacterium, one *Aspergillus fumigatus,* and one *Mycobacterium tuberculosis;* †HCAP: one atypical mycobacterium, one *M tuberculosis*.

***Table*: Frequency of microbial pathogens associated with community-acquired, health-care-associated, or hospital-acquired pneumonia**

pneumonia, both epidemiologically and microbiologically.

We declare that we have no conflicts of interest.

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4 Shorr AF, Zilberberg MD, Micek ST, Kollef MH. Prediction of infection due to antibiotic-resistant bacteria by select risk factors for health care-associated pneumonia. *Arch Intern Med* 2008; **168:** 2205–10.

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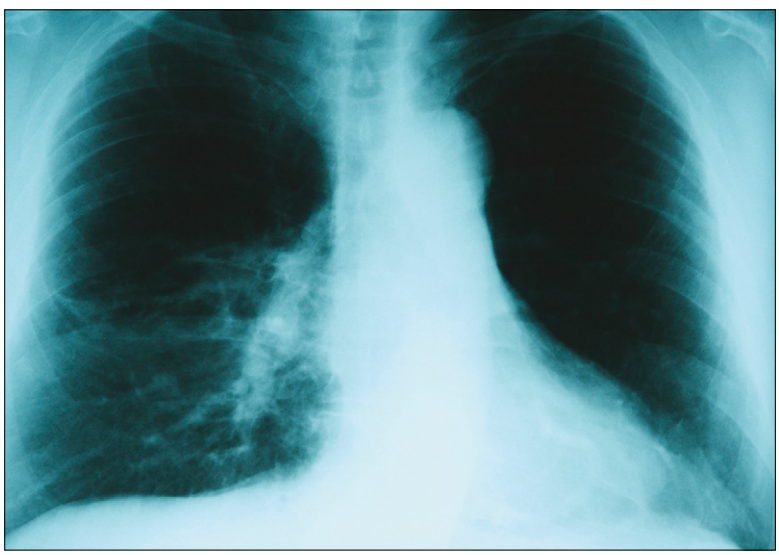
Authors' reply

We appreciate that Mario Venditti and colleagues now present their microbiological data for the Italian multicentre study of community-acquired, hospital-acquired, and health-care-assisted pneumonia (HCAP).[1] They claim that these data support the idea that HCAP is distinct from community-acquired pneumonia, a view with which we disagree. Microbiological data included samples from patients from the first 5 days after admission to hospital or within 5 days of diagnosis with pneumonia. Standards generally indicate that samples should be obtained at diagnosis. Results from samples obtained after diagnosis carry a significant risk for representing nosocomial colonisation or superinfection, particularly after introduction of antimicrobial treatment. This risk is a concern, particularly in view of the failure to undertake quantitative cultures of respiratory samples retrieved bronchoscopically. Overall, the diagnostic yield was low, with an aetiological diagnosis obtained in only 81 patients (22·4%). Of these 81, two had *Mycobacterium tuberculosis* and two had non-tuberculous mycobacteria, which are not usually regarded as pathogens of pneumonia. Of the patients with HCAP, only 28 had an aetiological diagnosis (26 excluding mycobacteria), which preclude valid conclusions about the aetiology of the populations studied.



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Classification of pneumonia on the basis of where it was acquired is under debate

The microbial range is statistically significant for only *Streptococcus pneumoniae*, which were more frequent in community-acquired pneumonia, and for meticillin-resistant *Staphylococcus aureus* (MRSA), which were more common in health-care-associated and hospital-acquired pneumonia. However, reported rates of MRSA are excessively high, reaching 17·1% even in community-acquired pneumonia, and if representative, would need guidelines of community-acquired pneumonia to be revised immediately. Moreover, caution should be taken when results of MRSA cultures are interpreted. In the absence of quantitative cultures, only bacteraemic episodes, or positive cultures from sites that are normally sterile, would be definite evidence for infection. *Pseudomonas aeruginosa* was even slightly higher in community-acquired than in hospital-acquired pneumonia (9·7% *vs* 7·1%), and Gram-negative enterobacteriaceae were more frequent in HCAP than in hospital-acquired pneumonia (32·1 *vs* 16·7). The unusually high rates of *P aeruginosa* and Gram-negative enteric bacilli in community-acquired pneumonia add to our reservations about the validity of the microbiological data. The investigators do not provide data for resistance patterns of *P aeruginosa* and Gram-negative enteric bacilli; we cannot therefore know the true rate of multidrug-resistant pathogens, although they claim to have identified an excessive rate of multidrug resistance in patients meeting the definition for HCAP.

Venditti and colleagues try to convince us that HCAP is different from community-acquired pneumonia with just 22 patients (11 with MRSA, two with *P aeruginosa*, nine with